URINARY IMMUNOGLOBULIN G, C-REACTIVE PROTEIN AND RETINOL BINDING PROTEIN AS CANDIDATE EARLY BIOMARKERS FOR RENAL DYSFUNCTION IN DOGS WITH PYOMETRA

B.E.J. Maddens[1], S. Daminet[2], P. Smets[2], K. Demeyere[1], H. de Rooster[2], E. Meyer[1].
[1]Department of Pharmacology, Toxicology, Biochemistry and Organ Physiology
[2]Department of Medicine and Clinical Biology of Small Animals, both Faculty of Veterinary Medicine, Ghent University, Belgium.

Renal dysfunction in dogs has been associated with pyometra. Nevertheless, the mechanism and type of renal injury remain controversial. Routine measurement of serum urea nitrogen and creatinine detects renal injury only in a late irreversible stage and does not indicate the localisation of the damage. We hypothesize that urinary immunoglobulin G (uIgG), C-reactive protein (uCRP) and retinol binding protein (uRBP) may serve as superior renal biomarkers. Both IgG and CRP are high molecular weight proteins indicating glomerular lesions, whereas RBP may serve as a tubular damage marker.

In this study, 14 dogs with *Escherichia coli* (*E. coli*) pyometra (P) without concurrent other diseases were included. Age-matched clinically healthy bitches (H) served as controls (n=14). At ovariohysterectomy (P, H) or ovariectomy (H) blood, urine and uterine swabs were taken. Serum biochemical analysis, CBC, urinanalysis and uterine bacteriological culture were performed. Commercial canine ELISAs were validated and used to quantify uIgG and uCRP; uRBP concentrations were determined with a human RBP ELISA kit validated for use in the dog. All concentrations were related to urinary creatinine concentration (uC) and expressed as ratios.

In P dogs, uIgG/C (196 ± 45.2 mg/g) and uCRP/C (706 ± 298 µg/g) (mean ± SEM) ratios were significantly increased compared to those in H bitches (2.1 ± 0.4 mg/g respectively 0.1 ± 0.1 µg/g) ($P<0.01$). Furthermore, uRBP/C ratios were significantly higher in P (43.7 ± 10.1 µg/g) than in H dogs (16.7 ± 5.5 µg/g) ($P<0.05$). A positive correlation at the 0.05 level was found between the urinary concentrations of all three proteins. Urinary total protein/C ratios (uTP/C) were significantly higher in P (0.77 ± 0.19) than in H dogs (0.16 ± 0.06) ($P<0.05$). A highly significant positive correlation was found between uTP/C and uIgG/C (R = 0.79) or uCRP/C (R = 0.72), but not between uTP/C and uRBP/C.

Concentrations of uIgG and uCRP, the latter for the first time examined in the dog, are strongly elevated in P bitches indicating glomerular dysfunction immediately after *E. coli* pyometra. The milder increase in uRBP is suggestive for tubular dysfunction, possible secondary to the proteinuria related to immune-mediated glomerulonephritis. We suggest that the observed increases in the candidate renal markers uIgG, uCRP and uRBP might be indicative of renal dysfunction at the glomerular and tubular level, associated with *E. coli* pyometra.